

30 MAR 2005

**PATENT COOPERATION TREATY**  
**PCT**  
**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

(PCT Article 36 and Rule 70)

REC'D 08 FEB 2005
WIPO PCT

Applicant's or agent's file reference JC217403/142	<b>FOR FURTHER ACTION</b>	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416).
International Application No. <b>PCT/NZ2003/000225</b>	International Filing Date (day/month/year) 8 October 2003	Priority Date (day/month/year) 8 October 2002
International Patent Classification (IPC) or national classification and IPC <b>Int. Cl. <sup>7</sup> C07C 237/30, 309/66, 311/39; C07D 263/04, 295/13; A61K 31/18, 31/166, 31/357, 31/5375; A61P 35/00.</b>		
Applicant <b>AUCKLAND UNISERVICES LIMITED et al.</b>		

<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 5 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e., sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p style="padding-left: 40px;">These annexes consist of a total of    sheet(s).</p>																								
<p>3. This report contains indications relating to the following items:</p> <table style="width: 100%; border: none;"> <tr> <td style="width: 5%; text-align: right;">I</td> <td style="width: 5%; text-align: center;"><input checked="" type="checkbox"/></td> <td>Basis of the report</td> </tr> <tr> <td>II</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Priority</td> </tr> <tr> <td>III</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td>IV</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Lack of unity of invention</td> </tr> <tr> <td>V</td> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td>VI</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Certain documents cited</td> </tr> <tr> <td>VII</td> <td style="text-align: center;"><input type="checkbox"/></td> <td>Certain defects in the international application</td> </tr> <tr> <td>VIII</td> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Certain observations on the international application</td> </tr> </table>	I	<input checked="" type="checkbox"/>	Basis of the report	II	<input type="checkbox"/>	Priority	III	<input type="checkbox"/>	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	IV	<input type="checkbox"/>	Lack of unity of invention	V	<input checked="" type="checkbox"/>	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	VI	<input type="checkbox"/>	Certain documents cited	VII	<input type="checkbox"/>	Certain defects in the international application	VIII	<input checked="" type="checkbox"/>	Certain observations on the international application
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Date of submission of the demand 21 January 2004	Date of completion of the report 21 January 2005
Name and mailing address of the IPEA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaaustralia.gov.au Facsimile No. (02) 6285 3929	Authorized Officer  <b>MARIE-ANNE FAM</b> Telephone No. (02) 6283 2254

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/NZ2003/000225**I. Basis of the report****1. With regard to the elements of the international application:\***

- ☒ the international application as originally filed:
- ☐ the description, pages , as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☐ the claims, pages , as originally filed,  
pages , as amended (together with any statement) under Article 19,  
pages , filed with the demand,  
pages , received on with the letter of
- ☐ the drawings, pages , as originally filed,  
pages , filed with the demand,  
pages , received on with the letter of
- ☐ the sequence listing part of the description:  
pages , as originally filed  
pages , filed with the demand  
pages , received on with the letter of

**2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.**

These elements were available or furnished to this Authority in the following language which is:

- ☐ the language of a translation furnished for the purposes of international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of the translation furnished for the purposes of international preliminary examination (under Rules 55.2 and/or 55.3).

**3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:**

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

**4. ☐ The amendments have resulted in the cancellation of:**

- ☐ the description, pages
- ☐ the claims, Nos.
- ☐ the drawings, sheets/fig.

**5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).\*\***

\* Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17).

\*\* Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

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## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)	Claims 1-21	YES
	Claims -	NO
Inventive step (IS)	Claims -	YES
	Claims 1-21	NO
Industrial applicability (IA)	Claims 1-21	YES
	Claims -	NO

## 2. Citations and explanations (Rule 70.7)

Novelty/Inventive Step

The following documents were cited in the International Search Report:

D1 Abstract 138:331354

D2 Journal of Medicinal Chemistry

D1 was published prior to the international filing date of the present application, but later than the priority date claimed. Under PCT guidelines, this document is excluded from consideration during international preliminary examination, however D1 is nevertheless included here for the purpose of information. This is based on the assumption that the claimed priority date is valid. Should this date subsequently be found invalid, then D1 may become relevant during national examination.

The present invention relates to nitroaniline-based unsymmetrical mustard analogues and their use in gene-dependent enzyme prodrug therapy (GDEPT).

D2 discloses various nitroaniline-based derivatives, which also find use in GDEPT. Compound 6 of this document falls within the scope of the present formula (I), but has been excluded from the claims by virtue of the proviso. Claims 1-21 are therefore novel.

However, claims 1-21 are considered to lack an inventive step in view of D2. As previously indicated, this document discloses the synthesis of the unsymmetrical analogue, compound 6. Given this information, it would be a routine matter for the skilled addressee to prepare other unsymmetrical nitroaniline derivatives.

The applicant has stated that compound 6 was described 'as not sufficiently potent for a full biological evaluation to be conducted' (see page 2, lines 21-24 of the specification). Whilst this comment is acknowledged, it is noted that the  $IC_{50}$  ratio obtained for this substance ( $>295$ ; see D2, page 1272, table 1) is comparable to, and in some cases greater than, the  $IC_{50}$  ratio for some of the compounds of the present invention (see page 39 of the specification, table 2).

In the absence of any indication that the present nitroaniline derivatives possess some unexpected property or advantage over the prior art, claims 1-21 cannot be considered inventive.

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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

- 1 Claim 1 lacks clarity. The claim makes reference to the situation wherein  $R^1$ ,  $R^4$  and  $R^5$  represent a tertiary amine (see page 42, lines 10-11 and lines 19-20). However this is inconsistent with the preceding definition of  $R^1$ ,  $R^4$  and  $R^5$ , wherein these groups are limited to optionally substituted alkyl.

A similar objection applies to claim 6.

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**Supplemental Box**

(To be used when the space in any of the preceding boxes is not sufficient)

**Continuation of Box V**

**Industrial Applicability**

Claims 1-21 meet the requirements for industrial applicability.